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Left Atrial Thrombus Associated With Ablation for Atrial Fibrillation: Identification With Intracardiac Echocardiography

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OBJECTIVES This study reports the incidence of, risk factors for, and management of left atrial (LA) thrombus documented by intracardiac echocardiography (ICE) during LA ablation for atrial fibrillation (AF).

BACKGROUND Thrombus formation is a risk associated with LA ablation procedures.

METHODS Intracardiac echocardiography imaging was performed in 232 patients (184 men, average age 55 ± 11 years) with AF undergoing pulmonary vein ostial ablation.

RESULTS Anticoagulation (activated clotting time >250 s) was maintained after dual transseptal catheterization. Left atrial thrombus (n = 30) was observed in 24 of 232 patients (10.3%). Thrombi measured 12.9 ± 11.1 mm (length) and 2.2 ± 1.3 mm (width) and were attached to a sheath or mapping catheter. Most thrombi (27 of 30, 90%) were eliminated from the LA by withdrawal of the sheath and catheter into the right atrium (RA). Two thrombi became wedged in the interatrial septum and incompletely withdrawn into the RA, and one was recognized only on post-procedure review of ICE images. Patients with LA thrombus had an increased LA diameter (4.8 ± 0.5 vs. 4.5 ± 0.6 cm, $p < 0.02$), spontaneous echo contrast (67% vs. 3%, $p < 0.0001$) and a history of persistent AF (29% vs. 6%, $p < 0.0002$). Multivariate discriminant analysis showed that spontaneous echo contrast ($f = 97.9$, $p < 0.0001$) was the most important determinant of LA thrombus formation. No patient with LA thrombus suffered a clinical thromboembolic complication.

CONCLUSIONS Left atrial thrombus identified on ICE may occur during LA catheter ablation procedures despite aggressive anticoagulation. Spontaneous echo contrast may predict risk for LA thrombus formation. Left atrial thrombus may be successfully withdrawn into the RA under ICE imaging with no overt complications. (J Am Coll Cardiol 2004;43:1861–7) © 2004 by the American College of Cardiology Foundation

Radiofrequency (RF) catheter ablation is an effective therapy for the treatment of many cardiac tachyarrhythmias. One of the major complications associated with RF ablation is the risk of thromboembolism. The reported incidence of thromboembolic complications during ablation procedures is 0.6%, increasing to 1.8% to 2% during left heart procedures (1). Limited data exist regarding the risk of more complicated left heart procedures such as ablation of atrial fibrillation (AF) (2). Intracardiac echocardiography (ICE) can detect and monitor left atrial (LA) thrombus (3). This study is designed to report the incidence, associated risk factors, and outcome of our initial experience managing LA thrombus during catheter ablation.

METHODS

Patient characteristics. From September 2000 to December 2002, 232 patients (184 men and 48 women; mean age 55 ± 11 years, range 17 to 80) underwent isolation of at least one pulmonary vein (PV) ostium for treatment of focal paroxysmal (n = 212) or persistent (n = 20) AF refractory to antiarrhythmic medications (Table 1). All patients gave written informed consent. All procedures followed the institutional guidelines of the University of Pennsylvania Health System. Cardiovascular disease was present in 91 patients (hypertension in 70, coronary artery disease in 16, mild aortic stenosis in 4, and prior resection of a LA myxoma in 1). All others had no structural heart disease demonstrated by history, stress imaging, and transthoracic/transesophageal echocardiographic study. Patients were routinely anticoagulated before the catheter ablation with long-term coumadin therapy. As a result, 90% of the patients were taking coumadin before the ablation procedure. All patients were admitted the day before the procedure for continuous heparin administration to achieve a partial thromboplastin time of 60 to 80 s. In addition, 325 mg of aspirin was administered on the morning of the planned ablation procedure.

Imaging system and technique. All ablation procedures were guided by ICE. Intracardiac echocardiography imaging was performed using a Sequoia diagnostic ultrasound catheter (5.5 to 10 MHz, 10 F). The ICE tip contains a 64-element vector phased-array transducer scanning in the

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Abbreviations and Acronyms

ACT = activated clotting time
AF = atrial fibrillation
ICE = intracardiac echocardiography
LA = left atrial/atrium
LVEF = left ventricular ejection fraction
PV = pulmonary vein
RA = right atrium
RF = radiofrequency

longitudinal monoplane. It provides a 90° sector two-dimensional and M-mode image and pulsed/continuous Doppler and color flow imaging with tissue penetration up to a depth of 16 cm. During each procedure, the ICE catheter was inserted into the femoral vein through an 11 F introducer sheath and advanced into the right atrium (RA). As previously described, ICE imaging was used to guide transseptal catheterization, assist positioning of the mapping and ablation catheters at the PV ostium, measure PV ostial flow before and after RF lesions, and monitor for possible complications (3,4). During ablation procedures, thrombus formation in the LA was monitored continuously online with ICE imaging by a dedicated operator for all but one patient. If a thrombus was documented, the timing of its development and its size, location, and outcome were noted.

For this study, spontaneous echo contrast, defined as slowly swirling non-homogeneous amorphous echoes in the LA (Fig. 1), was specifically evaluated with ICE at 7.5 MHz and was distinguishable from background noise or speckle by manipulation of gain settings before and during the ablation procedure.

Mapping and ablation procedure. Our mapping and ablation techniques have been previously described (4–6). Briefly, multipolar catheters were placed in the RA and in the coronary sinus for recording and internal cardioversion. Dual transseptal catheterization with ICE imaging guidance was performed to place two 8F Mullins sheaths and position through the sheaths a circular multipolar mapping catheter (Lasso) and an ablation catheter (Navistar, Biosense Webster, Diamond Bar, California) within the LA. Pulmonary vein isolation was achieved by applying RF energy to the LA/PV junction (4). Radiofrequency energy (up to 40 W, 52°C, and 90 s) was deployed at each targeted PV ostium and the surrounding LA wall until electrical isolation of PV from LA was achieved. All patients were anticoagulated with heparin after initial catheter placement. A bolus of 5,000 to 8,000 U of heparin was routinely administered immediately after transseptal puncture, followed by a continuous infusion of 1,000 to 1,500 U/h. Heparin dosing was guided based on weight, with 5,000 to 6,000 U followed by 1,000 to 1,200 U/h infusion for weight <100 kg and 7,000 to 8,000 U followed by 1,300 to 1,500 U/h for weight >100 kg. Activated clotting times (ACT) between 250 and 300 s were confirmed at 15 min after initial bolus and at 30-min intervals. An additional heparin bolus of 1,000 to 3,000 U was administered for any ACT values <250 s. All LA sheaths were continuously flushed with heparinized solution at >200 cc/h.

Management of LA thrombus. After ICE recognition of LA thrombus the following management strategy was deployed: 1) Anticoagulation status was confirmed, and additional heparin was administered as a bolus and continuous infusion to achieve an ACT >300 s. 2) The sheath and catheter on which thrombus was identified were immediately withdrawn into the RA as a single unit under careful ICE imaging monitoring. 3) If complete withdrawal into the RA was noted, the catheter and/or sheath were removed from the body under careful hemodynamic and oxygen saturation monitoring. 4) In all but the first patient the sheath and/or catheter was replaced and readvanced into the RA, and catheters (without sheath support) were re-advanced into the LA using appropriate catheter exchange and manipulation techniques to continue the procedure. 5) A decision to abort the ablation procedure and not recross into the LA was left to the electrophysiologist but was typically based on failure to remove

Table 1. Clinical, Echocardiographic, and Procedural Variables in Patients With and Without LA Thrombus Formation

	No LA Thrombus	LA Thrombus	p
Age (yrs)	55 ± 11	52 ± 11	NS
Gender (male/female)	165/43	19/5	NS
Underlying heart disease (%)	39.9 (83/208)	33.3 (8/24)	NS
Previous embolic event (%)	3.8 (8/208)	0	
Persistent AF (%)	6.7 (13/195)	29.2 (7/24)	< 0.0002
AF duration (yrs)	6.7 ± 6.0	6.9 ± 3.3	NS
Unsuccessful drugs	3.7 ± 1.9	3.5 ± 1.8	NS
LVEF (%)	56 ± 10	51 ± 11	NS
LA diameter (cm)	4.5 ± 0.6	4.8 ± 0.5	< 0.02
LA diameter/LVEF(cm × 100)	8.4 ± 2.7	9.8 ± 3.0	NS
Spontaneous echo contrast (%)	3.4 (7/208)	66.7 (16/24)	< 0.0001
Number of isolated PV/patient	3.1 ± 1.1	3.4 ± 1.0	NS
Acute successful PV isolation (%)	98.6 (205/208)	87.5 (21/24)	< 0.002

AF = atrial fibrillation; LA = left atrial; LVEF = left ventricular ejection fraction; NS = not significant; PV = pulmonary vein.

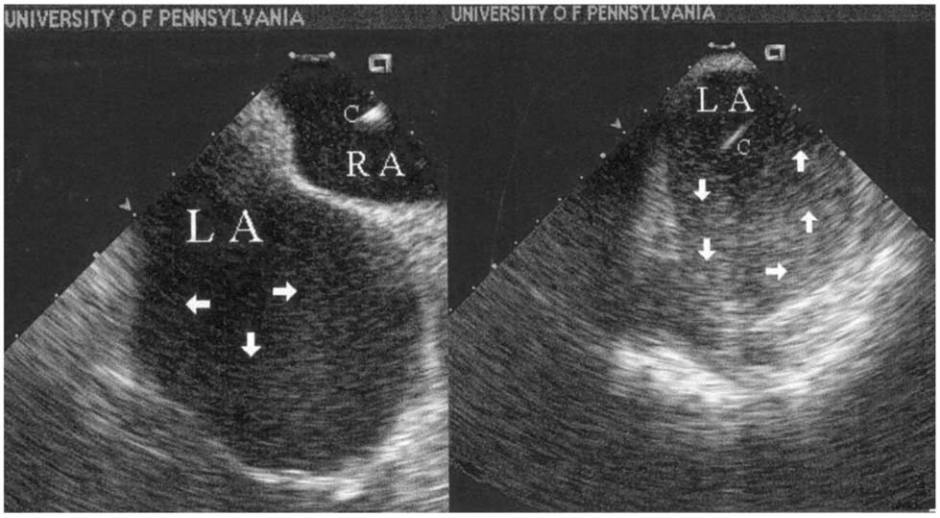

Figure 1. Intracardiac echocardiography images with the transducer (7.5 MHz) placed in the right atrium (RA) demonstrate spontaneous echo contrast, as slowly swirling amorphous echoes in a dilated (diameter = 5.2 cm) left atrium (LA) **(left panel)**. Slowly swirling non-homogeneous echoes become more prominent during sheath flushing with heparinized solution **(right panel)**.

thrombus completely into the RA or recurrence of thrombus after continuing the procedure.

Statistical analysis. Measurements are expressed as mean ± SD. Statistically significant differences for clinical, echocardiographic, and procedural variables between the LA thrombus and non-thrombus formation patient groups were determined using unpaired *t* test or chi-square test as appropriate. To further identify predictors of LA thrombus formation, all variables were subjected to a multivariate stepwise discriminant analysis (NCSS 2001) in which independent variables were considered candidates for forward entry into the function if their association with LA thrombus formation and their contribution to the selection function were significant ($p < 0.15$). A p value of <0.05 was considered statistically significant.

RESULTS

Incidence, timing, and characteristics of LA thrombus formation. Left atrial thrombus (n = 30) was observed with ICE imaging in 24 of 232 patients (10.3%). Repeat thrombus formation (i.e., recurrence after sheath/catheter removal from body and reinsertion of catheter into the LA) was observed once in four patients and twice in one patient despite maintaining ACT to >300 s. Left atrial thrombi occurred before RF energy application in 12 of the 24 patients (50%) and were noted 35 ± 24 (range 6 to 87) min after transseptal catheterization in that group. In the remaining 12 patients, LA thrombi occurred after starting RF energy application at 166 ± 60 (range 92 to 299) min after transseptal catheterization and 79 ± 56 (range 1 to 168) min after starting RF energy application.

Thrombus formation in both groups was not associated with RF energy delivery. The thrombi were characteristically single, linear, and mobile. Thrombi were attached to a sheath in 17 patients or Lasso catheter in 13 patients and were never noted to be attached to the ablation catheter (Fig. 2). Left atrial thrombi attached to the sheath were at the distal end of the sheath in 13 patients and at 20 ± 16 (3 to 38) mm proximal to the end of sheath in four patients; thrombi attached to the Lasso catheter were at the distal end of the shaft in five patients and at 16 ± 10 (5 to 35) mm proximal to the end of the shaft in eight patients. No mural or mobile thrombus attached to any RF lesion was observed under ICE imaging monitoring. The thrombi measured 12.9 ± 11.1 mm (range 3 to 40 mm) in maximal length and 2.2 ± 1.3 mm (range 0.5 to 5.8 mm) in maximal width.

Management of LA thrombus formation. Twenty-seven of the 30 thrombi (90%) were immediately eliminated from the LA by withdrawal of the sheath and catheter because they were firmly attached to the sheath or catheter. Intracardiac echocardiography imaging confirmed withdrawal into the RA (Fig. 2). Two thrombi were wedged into the interatrial septum with a small residual end in the LA as a result of attempted withdrawal into the RA. Reassessment with ICE at 24 h after maintaining ACT >300 s documented resolution of one thrombus and marked reduction in size of another (Fig. 3). The remaining thrombus occurred during the single procedure without a primary echo operator and was not detected until a retrospective review of recorded images after procedure. Documentation of removal to the RA was not confirmed in this patient. Of note, although thrombi were identified to be withdrawn completely from the LA into the RA in most patients, thrombi were recovered outside the body in only 8 of 30 patients. The gross appearance of the thrombotic material was as a strand of gelatinous material, which was not the characteristic char related to RF energy application. In the remaining thrombi we assumed that the thrombi had dislodged in the venous system during withdrawal. Importantly, none of the patients developed any respiratory

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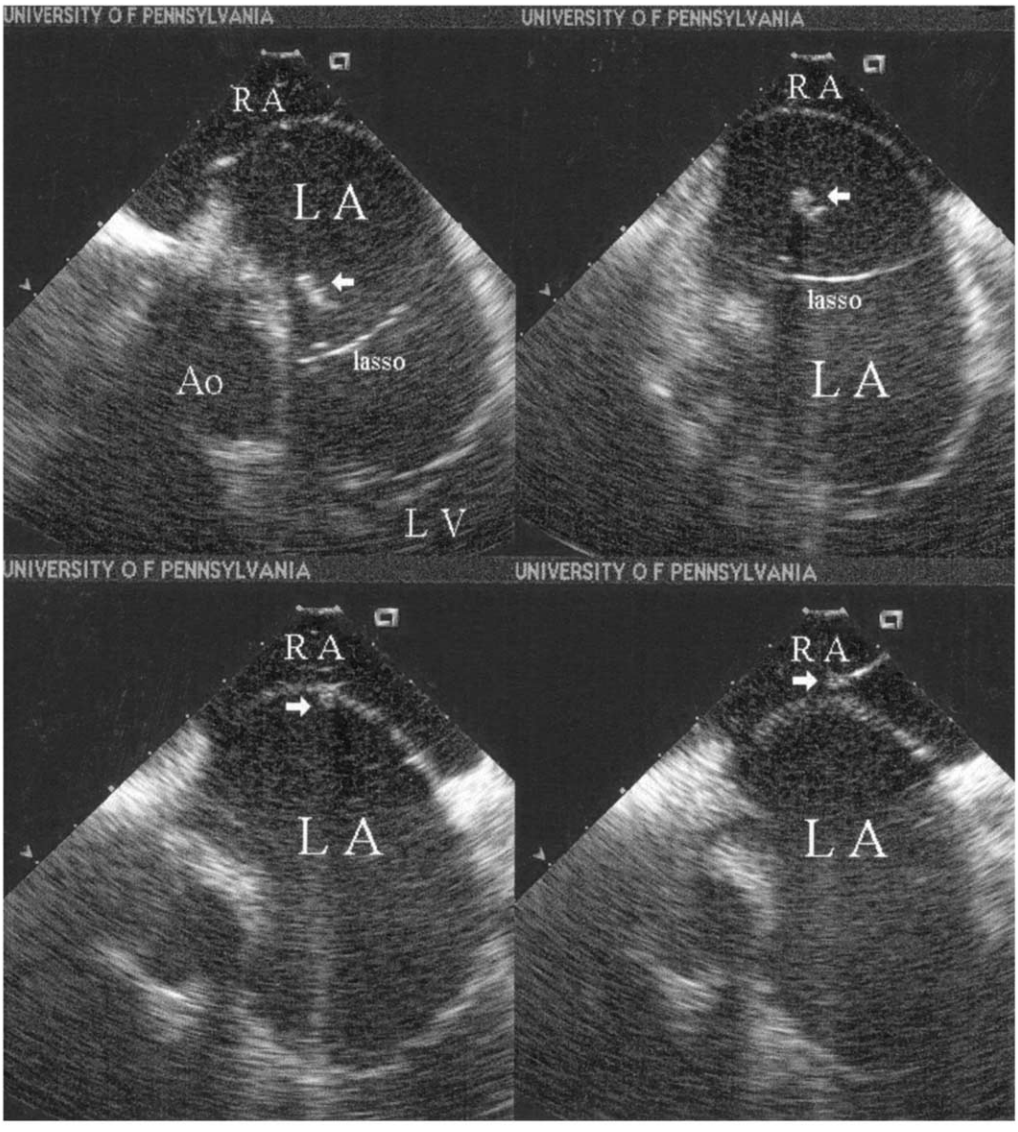

Figure 2. Intracardiac echocardiography images with transducer placed in the right atrium (RA) demonstrate a single, linear, and mobile thrombus (arrow, size 7.9 × 4.2 mm) attached at the sheath of lasso **(left upper panel)**, pulling the sheath/lasso with thrombus back **(right upper panel)** and withdrawal of thrombus from the left atrium (LA) **(left lower panel)** into the RA **(right lower panel)**. Ao = aorta; LV = left ventricle. Other abbreviations as in Figure 1.

compromise, drop in oxygen saturation, or change in hemodynamic status with the withdrawal of the catheters and sheaths.

The ablation procedure was terminated before isolation of all targeted PVs in three patients because of the thrombus wedging into the intraatrial septum (2 patients) and recurrent thrombus upon reinsertion of the catheters into the LA despite increase in ACT to >300 s (1 patient). In the remaining 21 patients mapping and ablation catheters were repositioned in the LA for completion of the ablation procedure. Additional thrombus formation was noted in four additional patients while we maintained an ACT >300 s as described, but completion of the ablation procedure had been achieved and thrombus was again safely withdrawn into the RA. During the entire procedure all patients had hemodynamic and continuous oxygen saturation monitoring besides the neurologic monitoring. The patients underwent neurologic examinations immediately after and then daily after the catheter ablation during the remainder of the characteristic three- to four-day hospitalization. All patients underwent a repeat evaluation during the four- to six-week follow-up visits. None of the patients in the study cohort with LA thrombus had any neurologic complaints, and the detailed neurologic examinations were always normal, indicating that no patient experienced a clinical intra/post-procedural thromboembolic complication (up to 10-month follow-up). No further diagnostic study, such as head CT or V/Q scan, was performed in the study cohort.

Factors predicting LA thrombus formation. Patient characteristics, ablation characteristics, and acute procedure outcome are listed in Table 1. Univariate analysis demonstrated that patients with LA thrombus formation had

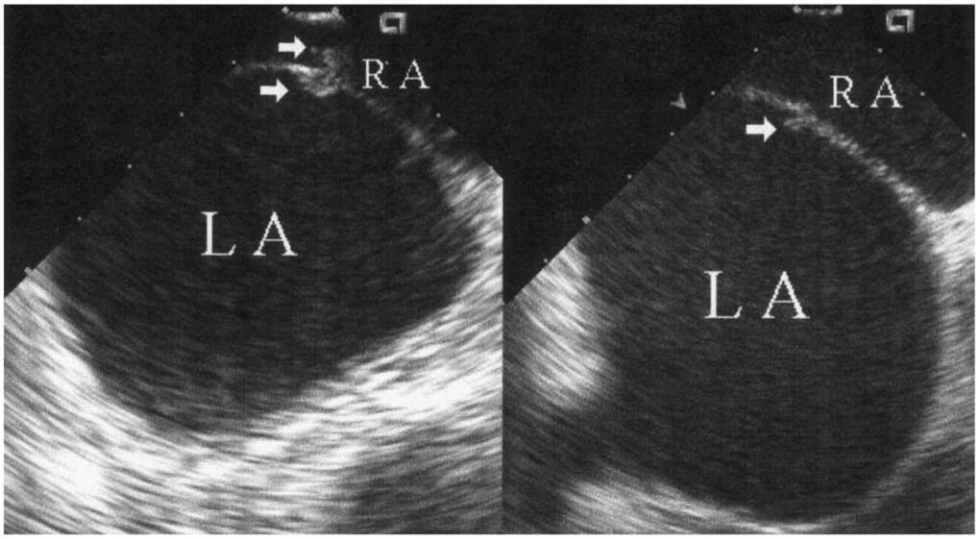

Figure 3. Intracardiac echocardiography images demonstrate LA thrombus (size 4.0 × 3.9 mm^2) wedged in the interatrial septum **(left panel)** and reduced in size (2.8 × 2.0 mm^2) under anticoagulation with follow-up images after 24 h **(right panel)**. Abbreviations as in Figure 1.

increased LA diameter (4.8 ± 0.5 vs. 4.5 ± 0.6 cm, $p < 0.02$), more prevalent spontaneous echo contrast (16 of 24 [67%] vs. 7 of 208 [3%], $p < 0.0001$) and persistent AF (7 of 24 [29%] vs. 13 of 208 [6%], $p < 0.0002$) compared to patients without thrombus formation. Interestingly, a history of previous thromboembolic events (8 patients) was noted only in patients without LA thrombus formation (Table 1). To further identify predictors of LA thrombus formation, 12 clinical, echocardiographic, and procedural variables listed in Table 1 were subjected to a stepwise multivariate discriminant analysis. Stepwise forward selection analysis of the variables showed that spontaneous echo contrast in LA ($f = 97.9$, $p < 0.0001$) was the most important determinant of LA thrombus formation. Nearly 70% (16 of 23) patients with evidence of spontaneous echo contrast developed an LA thrombus during the ablation procedure. Gender, age, underlying heart disease, history of embolic event, persistent AF, duration of AF, unsuccessful drugs ($f = 3.55$, $p = 0.07$), number of isolated PVs, LA diameter ($f = 1.12$, $p = 0.3$), and left ventricular ejection fraction (LVEF) ($f = 2.98$, $p = 0.091$) and their index (LA diameter/LVEF) ($f = 1.65$, $p = 0.21$) did not independently predict LA thrombus formation.

The ACT measurements in this study cohort indicated that there was no statistical difference for initial ACT values after the initial bolus of heparin between patients with LA thrombus (278 ± 27 s, range 222 to 316 s) and no thrombus formation (272 ± 29 s, range 202 to 319 s). In this study population, 99% of patients had ACT values documented to be >250 s within 30 min after the initial bolus of heparin. Any ACT values <250 s resulted in the immediate administration of heparin bolus (1,000 to 3,000 U) with subsequent ACT value >250 s confirmed within 15 min. Left atrial thrombus formation was not seen during such a transient value of ACT <250 s. No patient in this study cohort was noted to have ACT values consistently >300 s during the entire procedure.

DISCUSSION

The current report documents the ability of a phased-array ultrasound catheter to monitor in real time and detect thrombus formation in the LA during catheter ablation procedures for AF. Our study documents an unexpected higher incidence of ICE-documented LA thrombus formation of 10.3% during LA ablation related to presence of sheaths/catheters in a consecutive series of 232 patients with AF. The thrombus: 1) appears to commonly attach to the transseptal sheath and/or the circular mapping catheter (Lasso) despite anticoagulation with heparin to ACT >250 s; 2) appears to be firmly attached to sheath and/or catheter and can be typically withdrawn as a unit into the RA with a low risk of embolic events; and 3) appears most likely to develop in patients who demonstrate the presence of spontaneous echo contrast.

LA thrombus formation during AF ablation procedures. The reported incidence of systemic thromboembolic complications associated with RF catheter ablation in the left heart unrelated to AF has been reported to be as high as 2% (7). The risk of embolic stroke has been reported to be even higher, maybe as high as 5%, in targeting the triggers for AF with ablation (2). Thrombus formation may be due to activation of the coagulation cascade related to the placement of intravascular catheters and the duration of the ablation procedure (8). Another possibility is that thrombus is created by occasional tissue overheating, with energy application and coagulum formation acting as the nidus for more complex thrombus formation. The present study sheds light on the possible pathophysiology related to clot formation in the LA during the AF ablation procedure.

Left atrial thrombus formation occurred after transseptal

catheterization but before RF applications in 50% of patients. In the remaining patients, although thrombus formation was noted after RF ablation began, the LA thrombus firmly attached at a sheath or mapping catheter and not directly to the ablation catheter or to the PV ostia at the site of the ablation lesions. Furthermore, when the thrombus was found attached to the Lasso mapping catheter, the thrombus was always noted at the distal shaft, but not directly at the mapping electrodes. These observations suggest that the observed LA thrombus formation is not related to RF energy application. The common finding of thrombus formation only on the sheaths and/or circular mapping catheter shaft and not the ablation catheter was most likely due to their stable positioning for extended periods. In contrast, the ablation catheter tends to be continuously manipulated. Of note, a single ablation catheter technique used in a large series of AF ablation (589 patients) had no reported stroke complications (9). Because ICE was not used in this study, the possibility of thrombus formation in the LA on ablation catheter that is withdrawn into the RA and unrecognized must be considered. Obviously, one cannot exclude the possibility that thrombus formation may be due to intrinsic physical or component characteristics of the sheaths and circular mapping catheter. Importantly, all sheaths were managed with continuous infusion of heparinized saline at rates of >200 cc/h, so thrombus formation originating from stagnant flow surrounding the catheter was unlikely. This study provides a stimulus for the development of novel materials and anticoagulant coating on intravascular catheters and sheaths to prevent thrombus formation. In addition, different antithrombotic agents may influence the development of the thrombi, and more investigation is required in this area.

Of note, the time for the development of thrombus varied dramatically from 6 to 299 min after original transseptal sheath and catheter placement. No lapses in the maintenance of adequate heparinization were observed as a possible precipitant for thrombus formation, and thus a persistent risk throughout the procedure must be assumed. These data support the use of vigilant continuous online ICE monitoring to identify thrombus throughout the procedure. In contrast to mechanical radial imaging catheter with fixed ultrasonic frequency (10), the phased-array ultrasound catheter has a changeable ultrasonic frequency from 5.5 to 10 MHz, which provides detailed LA images with adequate imaging depth, even in patients with dilated LA.

Management of thrombus. Because the thrombus appeared to be firmly attached to the catheter/sheath in the LA during observation with ICE imaging monitoring, we attempted withdrawal of the thrombus-attached catheter/sheath from the LA to prevent any serious systemic embolic consequences. We were successful in doing so in all cases in which the thrombus was detected during the online monitoring. In two patients, however, the thrombus became wedged in the interatrial septal puncture site and did not remain attached to the catheter/sheath withdrawn into the RA. We maintained aggressive anticoagulation and documented the diminution and/or absence of thrombus after 24 h and no evidence of clinical embolic phenomenon. We believe that immediate withdrawal of the thrombus remains the best strategy because of the risk of thrombus dislodgement with persistent catheter manipulation required for successful PV isolation.

Of note, in most patients we could reinsert the catheters into the LA while maintaining an even higher ACT (>300 s) without additional thrombus formation. However, in five patients recurrent thrombus formation was noted; one of them had repeated thrombus formation identified on two separate attempts. It is interesting to speculate on whether maintaining an ACT >300 s or higher throughout the procedure may reduce the risk. The observed recurrences would suggest that the risk may not be definitely eliminated after a first thrombus, even with this greater degree of anticoagulation, and that vigilant monitoring with ICE may remain paramount.

Spontaneous echo contrast as risk predictor for LA thrombus formation. We document that spontaneous echo contrast in the LA is easily detected with ICE imaging. The opacification of the blood with spontaneous contrast effect usually appears as a swirling, "smoke-like" cloud (11). This phenomenon has been recognized for many years and occurs primarily with evidence of stagnant blood, especially with a large adynamic cardiac chamber. The mechanism for spontaneous echo contrast has not been fully elucidated but may include erythrocyte rouleaux formation and/or interaction of erythrocytes and fibrinogen modulated by shear forces (flow rate) (12–14). Some evidence suggests that LA spontaneous echo contrast may be a prothrombotic condition and a precursor to the development of a solid thrombus (7,15). Our results support a possible causal relationship. Given the high incidence of LA thrombus formation in 16 of 23 patients (70%) with spontaneous echo contrast during the ablation procedure, if ablation is expanded to chronic AF, spontaneous echo contrast will be even more common and thrombi may become common. Intracardiac echocardiography will assume more importance in this regard.

Study limitations. The number of study patients with LA thrombus formation during the AF ablation procedure was relatively small, and hence, the results with respect to the possibility of an embolic event during thrombus removal into the RA and predictors of thrombus formation should be interpreted with caution. Because no further diagnostic studies were performed, subclinical embolic events cannot be excluded, as fewer than a third of LA thrombi were physically removed from the patients. Clearly, there is a need for the development of strategies that might prevent the development of the thrombus so that treatment is not required. Increased intensity of anticoagulation (ACT >300 to 370 s) may reduce LA thrombus formation, especially in patients with spontaneous echo contrast (16). The small sample size may explain the lack of association

between previous thromboembolic events and LA thrombus formation. Moreover, patients with preexisting LA thrombus were excluded before the ablation procedure. In addition, we did not measure serum levels of fibrinogen or other plasma proteins to correlate with spontaneous echo contrast and thrombus formation during the ablation procedure. Future studies addressing this issue would be of interest.

Conclusions and clinical implications. Left atrial thrombus formation is seen in >10% of LA catheter ablation procedures for AF involving the use of long intravascular sheaths, multiple mapping, and ablation catheters. These thrombi can occur despite anticoagulation to ACT >250 s and careful sheath management with continuous heparinized solution infusion. Thrombi develop most commonly on sheaths and mapping (Lasso), but not ablation catheters. Spontaneous echo contrast in LA may predict LA thrombus formation. Left atrial thrombi may be successfully withdrawn into the RA under ICE imaging monitoring with no overt complications. These data are important in view of the increase in left heart interventional electrophysiologic procedures requiring multiple transseptal long sheath/catheter placement and the known risk of thromboembolic complications. The suggested management strategy with continuous ICE imaging monitoring may prevent or decrease LA thrombus complications.

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